

PHARMAMEDICAL TREND ANALYSIS (PMTA)



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Pharmacological Role of Andrographolide to Ameliorate Inflammatory Diseases and Cancers

Dr Md Anawar Hossain

Andrographolide has shown demonstrated therapeutic effect in inflammatory diseases, including liver diseases, joint diseases, respiratory system diseases, nervous system diseases, heart diseases, inflammatory bowel diseases, and inflammatory skin diseases. It also showed promising results in colorectal, liver, gastric, breast, prostate, lung, and oral cancers.

Various therapeutic effects of andrographolide

- Andrographolide is reported to have anti-bacterial, anti-viral, anti-inflammatory and anti-cancer functions (Vetvicka and Vannucci, 2021).
- It can also stimulate immune system and defense reactions.
- It is also evaluated in inflammation-mediated diseases, such as ulcerative colitis.
- Among the most pronounced activities are anti-bacterial and anti-tumor effects.
- Andrographolide demonstrated promising anti-cancer effects on different cancer diseases, such as colon cancer, breast cancer, head and neck carcinomas, prostate cancer and glioblastoma.
- Andrographolide protects against endothelial dysfunction and inflammatory response in rats with coronary heart disease by regulating PPAR and NF- κ B signaling pathways (Shu et al., 2020). Andrographolide may represent a medicinal approach for assessing and treating coronary heart disease.
- Luo et al. (2021) reported that Andrographolide exhibited significant protective effects against lung cancer. They provided new pharmacological insights based on high-throughput metabolomics analysis combined with network pharmacology.

Current problems in use of Andrographolide and further research

The natural extract from *Andrographis paniculata* plant has low solubility and low level of active substance. Therefore, it is needed to prepare chemical analogs.

- Although its therapeutic effects and molecular mechanisms of action are documented and partially characterized, further research is needed for more clear knowledge.
- The doses, types of treatment and possible negative side effects are not yet established.
- Currently, various isolations and compound formulas have been used for treatment of various diseases, making final conclusions problematic.

Adverse effects of *Andrographis paniculate*

About 100 medicines containing *Andrographis* are listed in the Australian Register of Therapeutic Goods (ARTG). Therefore, its side effects or adverse effects should be known by consumers and health professionals (TGA, 2020).

- It has potential to change sense of taste (TGA, 2020).

- The products containing the herb *Andrographis paniculata* may cause changes in the sense of taste, taste disturbance, and complete loss of taste.
- Consumers may take a couple of weeks to regain their normal taste after stopping the intake of this product.
- Healthcare professionals should inform the consumers about developing taste disturbances when using *Andrographis* products.



Fig. 1. Photograph of *Andrographis paniculata* Nees: Source from Intharuksa, A.; Aruntayanun, W.; Yoo-in, W.; Sirisa-ard, P. A Comprehensive Review of *Andrographis paniculata* (Burm. f.) Nees and Its Constituents as Potential Lead Compounds for COVID-19 Drug Discovery. *Molecules* 2022, 27, 4479.

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Leukaemia

Leukaemia is a type of blood cancer which occurs in the blood-forming tissue, usually the bone marrow. Leukaemia causes the over-production of abnormal white blood cells. Leukaemia affects white blood cells. Bone marrow can't produce the large numbers of normal blood cells which the body needs, because it becomes full of leukaemia cells. Generally, white blood cells fight against infection and disease and protect body.

- There is no obvious cause of leukaemia,
- It is not contagious,
- Leukaemia is not passed on from a parent to a child (inherited).

Age

People older than 55 are most often affected by leukemia occurrence. It is also the most common cancer in children younger than 15.

Major types of leukaemia are:

Acute lymphocytic leukaemia

This type of leukaemia is most commonly found in young children, but it can also affect the adult people.

Acute myelogenous leukaemia

This is a common type of leukaemia that affects both children and adults. But it is the most common type of acute leukaemia in adults.

Chronic lymphocytic leukaemia

It is the most common chronic leukemia in adult. The patient may feel well for years without needing treatment.

Chronic myelogenous leukemia

This type of leukemia mainly occurs in adults, who may have few or no symptoms for months or years before they move to a phase in which the leukaemia cells grow more quickly.

Other types – There are some other rarer types of leukemia which include hairy cell leukaemia, myelodysplastic syndromes and myeloproliferative disorders.

Symptoms of leukaemia

The leukaemia demonstrates variable symptoms relating to the type of leukaemia. The symptoms are often not clear or specific. Therefore, people overlook early leukaemia symptoms because the symptoms are similar to the symptoms of the flu and other common illnesses. Sometimes leukaemia is identified when people do their blood tests for some other disease or problems.

Common leukemia signs and symptoms include:

- Body temperatures increase or having fever,
- Feeling fatigue, weakness for long time,
- Shortness of breath, light-headedness, and palpitations,
- Having severe infections or frequent infections due to lack of normal white blood cells,
- Unexpected weight loss,
- Swollen lymph nodes in body,
- Bleeding or bruising more easily due to lack of platelets,
- Recurrent nosebleeds,
- Tiny red spots in skin (petechiae),
- Sweating more than normal, especially at night,
- Feeling bone pain or tenderness.

Treatment options of leukaemia are:

Chemotherapy

Drugs are used to kill cancer cell. In chemotherapy, steroids are normally used along with it for lymphoid leukaemia.

Radiation therapy

Radiation therapy is usually only for stem cell transplant or local disease e.g. in spleen.

Targeted therapy

Drugs are used to specifically recognise and kill leukaemia cells.

Biological therapy

In these treatments, the immune system is used to destroy leukaemia cells by using antibodies against markers on the leukaemia. These treatments used often monoclonal antibodies.

Stem cell transplant

A stem cell transplant (bone marrow transplant) is provided to younger/fitter patients. The patient's own healthy stem cells or stem cells from a donor can be used for this treatment. If chemotherapy does not cure the disease, then this treatment is used, most commonly for acute leukaemia.

Continuous Direct Compression Process for Low Dose Active Ingredients in a Solid Dosage Form

Dr Md Anawar Hossain

Continuous direct compression (CDC) can be a more suitable process to manufacture low-dose tablets. In addition, manufacturing by using a universal platform formulation seems to be a feasible way for producing low-dose products.

Introduction

Manufacturing low-dose solid dosage form encounters some challenging issues, because a homogenous distribution of active pharmaceutical ingredient (API) must be ensured to guarantee adequate end product quality (Ervasti et al., 2020). It is difficult to spread a small amount of API evenly into a big amount of excipient/excipients leading to heterogeneity in finished product potency. Adequate mixing can't make sure for a good blend quality due to the post-mixing handling process, which might cause segregation, i.e., de-mixing of materials. There are differences in the physical properties of particles of API and excipients, such as size, density and morphology, which are presumed to be the main factors causing segregation.

Continuous manufacturing process

Continuous manufacturing (CM) process has been under research, trial manufacturing and discussion for the last decade in pharmaceutical manufacturing. A lot of efforts of pharmaceutical companies have made this dream into reality and

as a result, at the beginning of 2020 there were several FDA- and EMA-approved products on the market which were being manufactured by continuous manufacturing process. However, a very small fraction of the total amount of marketed oral solid dosage products are manufactured by this process.

Drawbacks

The pharmaceutical companies are still now using batch manufacturing process, because they are not clear about the best strategies to apply CM processes in pharmaceutical manufacturing, i.e., for what types of products does it offer the greatest advantages?

Advantages of continuous manufacturing process

- The disadvantages of batch processes in manufacturing of low-dose products can be overcome.
- CM processing could be beneficial in manufacturing of low-dose products.
- The very low amount of material can be processed in CM line.
- The operators don't need to transfer large powder blends vertically into container, and thus decrease the risk of segregation during processing.
- Pneumatic transports, that also include free falls, are needed in certain cases in CM processing, but here also the tendency for de-mixing could be avoided by transporting only small quantities of blend within one cycle.
- In a direct compression process, there is, however, no need for any conveyors.
- Continuous mixing has been shown to be capable to produce more homogenous mixtures as compared to batch mixing,
- Therefore, a continuous direct compression (CDC) set-up is a reliable and excellent method for low-dose manufacturing.



- Karttunen et al. (2019) reported some promising results by comparing a CDC process with traditional batch manufacturing.
- The manufacturing line may be equipped with suitable process analytical technology

(PAT) tools, enabling the monitoring of API concentration during processing (and capability to reveal if problems are about to occur), makes it even more attractive.

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Product Quality: Prediction by Using Big Data in Pharmaceutical Manufacturing

Dr Md Anawar Hossain

Analysis of big data collected from the different steps of medicine manufacturing processes for long time helps the pharma industry to find alternative ways to determine their product quality.

Data analysis and product quality

The regulatory bodies encourage the pharmaceutical industry to use new digital technologies and better utilize the data collected to show the quality of their products and improvement of manufacturing efficiency. In the pharmaceutical industries, a lot of processes, machines and equipment are used to manufacture medicines. These machines are equipped with numerous sensors monitoring and controlling critical process and equipment parameters. Therefore, manufacturing of every medicine produces a large amount of data which are sourced from laboratory analysis of incoming raw materials, process parameters, intermediate product characteristics, complex compression process time series outputs available for every second of the manufacturing process and final product quality (Žagar and Mihelič, 2022). These databases are used to confirm the quality of incoming raw materials, intermediate products, and final products. They reported that the excipients, incoming materials and direct compression process have a significant impact on final product quality.

Conclusions

Žagar and Mihelič (2022) collected the data from three main databases: “Laboratory Sample Manager Database”, “Production database”, and “Process time series database connected with tablet press SQL database”. They reported that the data is highly valuable because it provides an insight into every 10 seconds of the process trajectory for 1005 actual production batches along with product quality collected over several years. They indicated that advanced analysis models can be developed using this dataset. In addition, this dataset can be used to determine product quality and develop procedures which would lead to the omission of current conventional and time-consuming laboratory testing.

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